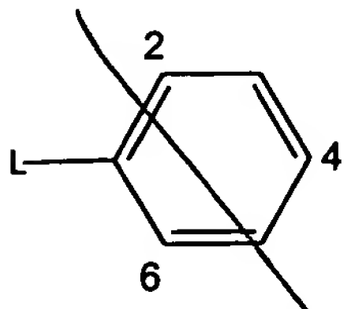


wherein L indicates a bond to the pyrimidine ring in Formula B

and the Ar phenyl group is substituted at one, two, or three of positions 2, 4, and 6 with substituents independently selected from:

i) halogen, cyano, halo($C_{1-4}$)alkyl, halo($C_{1-4}$)alkoxy, hydroxy, amino, $C_{1-6}$ alkyl, $C_{1-6}$alkoxy, ($C_{1-4}$alkoxy)$C_{1-4}$alkoxy, and mono- or di($C_{1-4}$alkyl)amino,

ii) $C_{1-6}$ alkyl and $C_{1-6}$alkoxy which are further substituted with a 3- to 7-membered carbocyclic and heterocyclic group, which is saturated, unsaturated, or aromatic, which 3- to 7-membered carbocyclic and heterocyclic group may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, $C_{1-4}$alkyl, -O($C_{1-4}$alkyl), -NH($C_{1-4}$alkyl), and -N($C_{1-4}$alkyl)($C_{1-4}$alkyl);

$R_X$ and $R_Y$ are the same or different and are independently selected from the group consisting of:

a) hydrogen (with the proviso that $R_x$ and $R_Y$ are not both hydrogen),

b) -(C=O)$alkyl_A$, wherein $alkyl_A$ is a straight or branched alkyl group having from 1 to 8 carbon atoms;

c) straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, (cycloalkyl)alkyl groups consisting of 4 to 12 carbon atoms, straight, branched, or cyclic alkenyl groups consisting of 2 to 8 carbon atoms, or straight or branched alkynyl groups consisting of 2 to 8 carbon atoms.

## REMARKS

The Applicants appreciate the Examiner's thorough examination of the subject application, the indication that claims 1, 2, 4, 24-30, and 35-68 are in a condition for allowance, and the indication that claims 7, 8, 22, and 23 would be in a condition for allowance if rewritten in independent form. Applicants further request reconsideration of the subject application based on the instant amendments and following remarks.

Claims 3, 9, 10, 13-15, 17, 19, and 20 have been amended. No new matter has been added by the claim amendments. Support for the amendment to claims can be found in the claims as originally filed and throughout the specification.

The specification has been amended to provide express support for claim 31 as originally filed. Although applicants believe that claim 31 was properly supported by the original specification, it is believed that the addition of the new paragraph at page 20, line 28 will make express that which previously had been implicit. No new matter has been introduced by the amendments to the specification.

Claims 3, 5, 6, and 9-21 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is believed the amendments made herein obviate the rejection. Accordingly, reconsideration and withdrawal of the rejection are requested.

The language "(cycloalkyl)alkyl consisting of 3 to 8 carbon atoms" has been amended to provide (cycloalkyl)alkyl groups consisting of between 4 and 12 carbon atoms. The amended language is fully supported by the specification. See, for example, page 24, lines 3 to 8 for a definition of the scope of carbon atoms present in "cycloalkyl" and "(cycloalkyl)alkyl)" groups.

In view thereof, reconsideration and withdrawal of the rejection are requested.

Claims 31-34 stand rejected under 35 U.S.C. § 112, first paragraph. As grounds for the rejection, the position is taken that:

"Said claims recite assay methods which do not appear to have description in the specification. Page 55 in the specification describe an assay method for CRF receptor binding. However, there is no mention of a "detectably-labeled compound or salt", nor is there a description of the step of "washing the tissue sample to remove unbound compound" as recited in claim 31. Likewise, the method in claim 32 has no description in the specification. Page 55 briefly describes the cell line of IMR-32, but provides no assay step involving such as cell line. Similarly, there does not appear to be a description of an *in-vivo* test that involves a neuronal cell, a brain cell or cerebrospinal fluid. It appears that the *in-vivo* test done was to determine cardiotoxicity and hepatotoxicity, rather than for the binding of CRF on neuronal cell, or brain cell. Thus, the methods claimed do not have description or support in the specification to guide one skilled in the art"

The rejection is traversed.

The application fully satisfies the requirements of 35 U.S.C. §112, including the requirements of Section 112, first paragraph.

Claim 31 provides a method of localizing CRF receptors is tissue section samples. The specification provides ample support for methods of localizing CRF receptors using a detectably-labeled compound. See, for example, the specification at page 56 (Example 97), page 5 at lines 24-27, and page 20 at lines 23-28. Applicants submit that the washing step of claim 31 is implicitly described by the specification such that one of ordinary skill in the art would fully comprehend the scope of the invention provided by the claims. Furthermore the specification provides an explicit example of how the washing step may be performed at page 54, lines 3-7.

However, in the interest of expediting prosecution, the specification has been amended to make explicit that which was previously implicit. Thus the new paragraph on page 20 combined with the disclosure in the specification at page 20, lines 23-28 and Examples 96 and 97 provide ample description in support of claim 31 as filed.

Support for claims 32 – 34 may also be found in the specification as filed. For instance, the specification as filed provides methods of inhibiting the binding of CRF to the CRF1 receptor

including *in vivo* methods of inhibition. See the specification as filed at page 20, line 29 to page 21, line 11.

In view thereof, reconsideration and withdrawal of the rejection are requested.

It is respectfully submitted that the subject application is in condition for allowance. Early and favorable action is requested.

Applicants believe that additional fees are not required for consideration of the within Response. However, if for any reason a fee is required, a fee paid is inadequate or credit is owed for any excess fee paid, you are hereby authorized and requested to charge Deposit Account No. **04-1105**.

Respectfully submitted,

Date: November 15, 2002

By: _____

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**317919**

DO NOT ENTER

**VERSION WITH CHANGES MARKED**

(Additions are underlined; deletions are bracketed.)

OF AMDT C

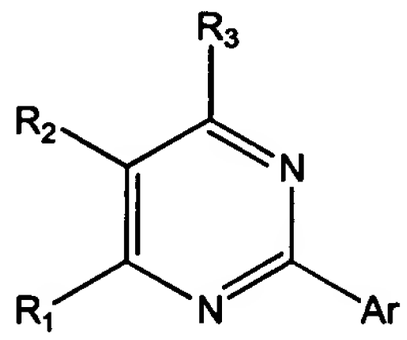
IN THE SPECIFICATION

Kindly add after the paragraph ending at page 20, line 28, the new paragraph as follows:

<u>The present invention also provides a method for localizing CRF receptors is tissue section samples comprising contacting with a sample of tissue a detectably-labeled compound or salt of Formula I under conditions that permit binding of the compound to CRF receptors within the sample of tissue, washing the tissue sample to remove unbound compound, and detecting remaining bound compound, wherein the detection of remaining bound compound is an indication of the presence of CRF receptors in the tissue sample.</u>

IN THE CLAIMS

3. (twice amended) A compound of the formula




or a pharmaceutically acceptable salt thereof, wherein:

$R_1$ and $R_3$ are independently selected from hydrogen, halogen, cyano, $C_{1-6}$ alkyl, $C_{2-6}$alkenyl, $C_{2-6}$alkynyl, $(C_{3-7}cycloalkyl_1)C_{1-4}alkyl$, $(C_{3-7}cycloalkyl_1)C_{2-4}alkenyl$, $(C_{3-7}cycloalkyl_1)$ $C_{2-4}$alkynyl, $-O(C_{3-7}cycloalkyl_1)C_{1-4}alkyl$, $-O(C_{3-7}cycloalkyl_1)C_{2-4}alkenyl$, $-O(C_{3-7}cycloalkyl_1)$ $C_{2-4}$alkynyl, halo$(C_{1-6})$alkyl, halo$C_{2-6}$alkenyl, halo$C_{2-6}$alkynyl, -O(halo$(C_{1-6})$alkyl), -O(halo$(C_{2-6})$alkenyl), -O(halo$(C_{2-6})$alkynyl), -O($C_{1-6}$alkyl), -O($C_{2-6}$alkenyl), -O($C_{2-6}$alkynyl), $S(O)_n(C_{1-6}alkyl$, $S(O)_n(C_{2-6}alkenyl)$, and $S(O)_n(C_{2-6}alkynyl)$,

where each alkyl, or alkenyl is independently straight, branched, or cyclic, and each alkynyl is straight or branched, and is optionally substituted with one or more substituents independently chosen from halogen, hydroxy, oxo, cyano, $C_{1-4}$alkoxy, amino, and mono- or di($C_{1-4}$)alkylamino,

and

where each $C_{3-7}$cycloalkyl$_1$ is optionally substituted by one or more substituents independently chosen from halogen, hydroxy, oxo, cyano, $C_{1-4}$alkoxy, amino, and mono- or di($C_{1-4}$)alkylamino,

with the proviso that not both $R_1$ and $R_3$ are hydrogen;

$R_2$ is selected from the group consisting of $-XR_A$ and Y; and

Ar is selected from the group consisting of phenyl, naphthyl, pyridyl, pyrimidinyl, pyridizinyl, and thiophenyl, each of which is mono-, di-, or tri-substituted with $R_C$;

$R_A$ and $R_B$, which may be the same or different, are independently selected at each occurrence from:

hydrogen, straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, (cycloalkyl)alkyl groups consisting of [3]4 to [8]12 carbon atoms, straight, branched, or cyclic alkenyl groups consisting of 2 to 8 carbon atoms, or straight or branched alkynyl groups consisting of 2 to 8 carbon atoms, each of which may be further substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, cyano, amino, $C_{1-6}$alkoxy, -NH($C_{1-6}$alkyl), -N($C_{1-6}$alkyl)( $C_{1-6}$alkyl), -NHC(=O)($C_{1-6}$alkyl), -N($C_{1-6}$alkyl)C(=O)($C_{1-6}$alkyl), -NHS(O)$_n$($C_{1-6}$alkyl), -S(O)$_n$($C_{1-6}$ alkyl), -S(O)$_n$NH($C_{1-6}$alkyl), -S(O)$_n$N($C_{1-6}$ alkyl)($C_{1-6}$alkyl), and Z;

$R_C$ is independently selected at each occurrence from halogen, cyano, halo($C_{1-6}$)alkyl, halo($C_{1-6}$)alkoxy, hydroxy, amino, $C_{1-6}$alkyl substituted with 0-2 $R_D$, $C_{2-6}$ alkenyl substituted with 0-2 $R_D$, $C_{2-6}$alkynyl substituted with 0-2 $R_D$, $C_{3-7}$cycloalkyl substituted with 0-2 $R_D$, ($C_{3-7}$cycloalkyl)$C_{1-4}$alkyl substituted with 0-2 $R_D$, $C_{1-6}$alkoxy substituted with 0-2 $R_D$, -NH($C_{1-6}$alkyl) substituted with 0-2 $R_D$, -N($C_{1-6}$alkyl)($C_{1-6}$alkyl) each $C_{1-6}$alkyl independently substituted with 0-2 $R_D$, $-XR_A$, and Y;

$R_D$ is independently selected at each occurrence from the group consisting of halogen, hydroxy, cyano, amino, $C_{1-4}$alkyl, -O($C_{1-4}$alkyl), -NH($C_{1-4}$alkyl), -N($C_{1-4}$alkyl)($C_{1-4}$alkyl), -S(O)$_n$(alkyl), halo($C_{1-4}$)alkyl, halo($C_{1-4}$)alkoxy, CO($C_{1-4}$alkyl), CONH($C_{1-4}$alkyl), CON($C_{1-4}$alkyl)( $C_{1-4}$alkyl), -$XR_A$, and Y;

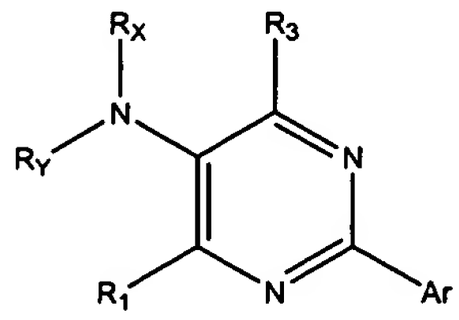
X is independently selected at each occurrence from the group consisting of -$CH_2$-, -$CHR_B$-, -O-, -C(=O)-, -C(=O)O-, -S(O)$_n$-, -NH-, -$NR_B$-, -C(=O)NH-, -C(=O)$NR_B$-, -S(O)$_n$NH-, -S(O)$_n$$NR_B$-, -OC(=S)S-, -NHC(=O)-, -$NR_B$C(=O)-, -NHS(O)$_n$-, -OSi$H_n$($C_{1-4}$alkyl$_{2-n}$-, and –$NR_B$S(O)$_n$-;

Y and Z are independently selected at each occurrence from: 3- to 7-membered carbocyclic or heterocyclic groups which are saturated, unsaturated, or aromatic, which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, cyano, $C_{1-4}$alkyl, -O($C_{1-4}$alkyl), -NH($C_{1-4}$alkyl), -N($C_{1-4}$alkyl)($C_{1-4}$alkyl),and -S(O)$_n$(alkyl),

said 3- to 7-memberered heterocyclic groups containing one or more heteroatom(s) independently selected from N, O, and S, with the point of attachment being either carbon or nitrogen; and

n is independently selected at each occurrence from 0, 1, and 2.

9. (twice amended) A compound of Formula A




Formula A

or a pharmaceutically acceptable salt thereof, wherein:

$R_X$ and $R_Y$ are the same or different and are independently selected from:

a) hydrogen,

b) -(C=O)$alkyl_A$, wherein $alkyl_A$ is a straight or branched alkyl group having from 1 to 8 carbon atoms;

c) straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, cycloalkyl(alkyl) groups consisting of [3]4 to [8]12 carbon atoms, straight, branched, or cyclic alkenyl groups consisting of 2 to 8 carbon atoms, or straight or branched alkynyl groups consisting of 2 to 8 carbon atoms, each of which may be further substituted with one or more substituent(s) independently selected from:

i) hydroxy, halogen, amino, cyano, -O($C_{1-4}$alkyl), -NH($C_{1-4}$alkyl), and -NH($C_{1-4}$alkyl)($C_{1-4}$alkyl), and

ii) 3- to 7-membered carbocyclic and heterocyclic groups, which are saturated, unsaturated, or aromatic, which may be substituted with one or more substituents independently selected from halogen, halo($C_{1-4}$)alkyl, halo($C_{1-4}$)alkoxy, oxo, hydroxy, amino, $C_{1-4}$alkyl, -O($C_{1-4}$alkyl), -NH($C_{1-4}$alkyl), –N($C_{1-4}$alkyl)($C_{1-4}$alkyl), and -$S(O)_n$(alkyl), wherein said 3- to 7-memberered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S, with the point of attachment being either carbon or nitrogen,

$R_1$ and $R_3$ are independently selected from hydrogen, halogen, cyano, $C_{1-6}$ alkyl, $C_{2-6}$alkenyl, $C_{2-6}$alkynyl, ($C_{3-7}$cycloalkyl$_1$)$C_{1-4}$alkyl, ($C_{3-7}$cycloalkyl$_1$)$C_{2-4}$alkenyl, ($C_{3-7}$cycloalkyl$_1$) $C_{2-4}$alkynyl, -O($C_{3-7}$cycloalkyl$_1$)$C_{1-4}$alkyl, -O($C_{3-7}$cycloalkyl$_1$)$C_{2-4}$alkenyl, -O($C_{3-7}$cycloalkyl$_1$) $C_{2-4}$alkynyl, halo($C_{1-6}$)alkyl, halo$C_{2-6}$alkenyl, halo$C_{2-6}$alkynyl, -O(halo($C_{1-6}$)alkyl), -O(halo($C_{2-6}$)alkenyl), -O(halo($C_{2-6}$)alkynyl), -O($C_{1-6}$alkyl), -O($C_{2-6}$alkenyl), -O($C_{2-6}$alkynyl), $S(O)_n$($C_{1-6}$alkyl, $S(O)_n$($C_{2-6}$alkenyl), and $S(O)_n$($C_{2-6}$alkynyl),

where each alkyl, or alkenyl is independently straight, branched, or cyclic, and each alkynyl is straight or branched, and is optionally substituted by one or more substituents independently chosen from halogen, hydroxy, oxo, cyano, $C_{1-4}$alkoxy, amino, and mono- or di($C_{1-4}$)alkylamino,

and

where said $C_{3-7}$cycloalkyl$_1$ is optionally substituted by one or more substituents independently chosen from halogen, hydroxy, oxo, cyano, $C_{1-4}$alkoxy, amino, and mono- or di($C_{1-4}$)alkylamino

with the proviso that not both $R_1$ and $R_3$ are hydrogen;

Ar is selected from the group consisting of phenyl, naphthyl, pyridyl, pyrimidinyl, and thiophenyl, each of which is mono-, di-, or tri-substituted with $R_C$;

$R_A$ and $R_B$, which may be the same or different, are independently selected at each occurrence from the group consisting of:

hydrogen, straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, (cycloalkyl)alkyl groups consisting of [3]4 to [8]12 carbon atoms, straight, branched, or cyclic alkenyl groups consisting of 2 to 8 carbon atoms, and straight or branched alkynyl groups consisting of 2 to 8 carbon atoms, each of which may be further substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, nitro, cyano, $C_{1-6}$alkoxy, -NH($C_{1-6}$alkyl), -N($C_{1-6}$alkyl)( $C_{1-6}$alkyl), -NHC(=O)($C_{1-6}$alkyl), -N($C_{1-6}$alkyl)C(=O)($C_{1-6}$alkyl), -NHS(O)$_n$($C_{1-6}$alkyl), -S(O)$_n$($C_{1-6}$ alkyl), -S(O)$_n$NH($C_{1-6}$alkyl), -S(O)$_n$N($C_{1-6}$ alkyl)($C_{1-6}$alkyl), and Z;

$R_C$ is independently selected at each occurrence from halogen, cyano, halo($C_{1-6}$)alkyl, halo($C_{1-6}$)alkoxy, hydroxy, amino, and $C_{1-6}$alkyl substituted with 0-2 $R_D$, $C_{2-6}$ alkenyl substituted with 0-2 $R_D$, $C_{2-6}$alkynyl substituted with 0-2 $R_D$, $C_{3-7}$cycloalkyl substituted with 0-2 $R_D$, ($C_{3-7}$cycloalkyl)$C_{1-4}$alkyl substituted with 0-2 $R_D$, $C_{1-6}$alkoxy substituted with 0-2 $R_D$, -NH($C_{1-6}$alkyl) substituted with 0-2 $R_D$, -N($C_{1-6}$alkyl)($C_{1-6}$alkyl) each $C_{1-4}$alkyl independently substituted with 0-2 $R_D$, -$XR_A$, and Y, with the proviso that at least one of the positions ortho or para to the point of attachment of Ar to the pyrimdine ring shown in Formula A is substituted;

$R_D$ is independently selected at each occurrence the group consisting of halogen, hydroxy, cyano, $C_{1-4}$alkyl, -O($C_{1-4}$alkyl), -NH($C_{1-4}$alkyl), -N($C_{1-4}$alkyl)($C_{1-4}$alkyl), -S(O)$_n$(alkyl) halo($C_{1-4}$)alkyl, halo($C_{1-4}$)alkoxy, CO($C_{1-4}$alkyl), CONH($C_{1-4}$alkyl), CON($C_{1-4}$alkyl)( $C_{1-4}$alkyl), -$XR_A$, and Y;

X is independently selected at each occurrence from the group consisting of -$CH_2$-, -$CHR_B$-, -O-, -C(=O)-, -C(=O)O-, -S(O)$_n$-, -NH-, -$NR_B$-, -C(=O)NH-, -C(=O)$NR_B$-, -S(O)$_n$NH-, -

$S(O)_nNR_B$-, -OC(=S)S-, -NHC(=O)-, -$NR_B$C(=O)-, -$NHS(O)_n$-, -$OSiH_n(C_{1-4}$-$alkyl_{2-n})$-, and –$NR_BS(O)_n$-;

Y and Z are independently selected at each occurrence from the group consisting of: 3- to 7-membered carbocyclic and heterocyclic groups, which are saturated, unsaturated, or aromatic, which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, $C_{1-4}$alkyl, -$O(C_{1-4}$alkyl), -$NH(C_{1-4}$alkyl), -$N(C_{1-4}$alkyl)($C_{1-4}$alkyl), and -$S(O)_n$(alkyl); and

n is 0, 1, or 2.

10. (twice amended) A compound or salt according to Claim 9, wherein:

$R_X$ and $R_Y$ are the same or different and are independently selected from:

a) -(C=O)$alkyl_A$, wherein $alkyl_A$ is a straight or branched alkyl group having from 1 to 8 carbon atoms;

b) straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, (cycloalkyl)alkyl groups consisting of [3]4 to [8]12carbon atoms, straight, branched, or cyclic alkenyl groups consisting of 2 to 8 carbon atoms, or straight or branched alkynyl groups consisting of 2 to 8 carbon atoms, each of which may be further substituted with one or more substituent(s) independently selected from:

i) hydroxy, halogen, amino, cyano, -$O(C_{1-4}$alkyl), -$NH(C_{1-4}$alkyl), and -$NH(C_{1-4}$alkyl)($C_{1-4}$alkyl), and

ii) 3- to 7-membered carbocyclic and heterocyclic groups, which are saturated, unsaturated, or aromatic, which may be substituted with one or more substituents independently selected from halogen, halo($C_{1-4}$)alkyl, halo($C_{1-4}$)alkoxy, oxo, hydroxy, amino, $C_{1-4}$alkyl, -$O(C_{1-4}$alkyl), -$NH(C_{1-4}$alkyl), –$N(C_{1-4}$alkyl)($C_{1-4}$alkyl), and -$S(O)_n$(alkyl), wherein said 3- to 7-memberered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S, with the point of attachment being either carbon or nitrogen,

$R_1$ and $R_3$ are independently selected from hydrogen, halogen, cyano, $C_{1-6}$ alkyl, $C_{2-6}$alkenyl, $C_{2-6}$alkynyl, ($C_{3-7}$cycloalkyl$_1$)$C_{1-4}$alkyl, ($C_{3-7}$cycloalkyl$_1$)$C_{2-4}$alkenyl, ($C_{3-7}$cycloalkyl$_1$) $C_{2-4}$alkynyl, -O($C_{3-7}$cycloalkyl$_1$)$C_{1-4}$alkyl, -O($C_{3-7}$cycloalkyl$_1$)$C_{2-4}$alkenyl, -O($C_{3-7}$cycloalkyl$_1$) $C_{2-4}$alkynyl, halo($C_{1-6}$)alkyl, halo$C_{2-6}$alkenyl, halo$C_{2-6}$alkynyl, -O(halo($C_{1-6}$)alkyl), -O(halo($C_{2-6}$)alkenyl), -O(halo($C_{2-6}$)alkynyl), -O($C_{1-6}$alkyl), -O($C_{2-6}$alkenyl), and -O($C_{2-6}$alkynyl),

where each alkyl, or alkenyl is independently straight, branched, or cyclic, and each alkynyl is straight or branched, and is optionally substituted by one or more substituents independently chosen from halogen, hydroxy, oxo, cyano, $C_{1-4}$alkoxy, amino, and mono- or di($C_{1-4}$)alkylamino,

and

where said $C_{3-7}$cycloalkyl$_1$ is optionally substituted by one or more substituents independently chosen from halogen, hydroxy, oxo, cyano, $C_{1-4}$alkoxy, amino, and mono- or di($C_{1-4}$)alkylamino

Ar is phenyl, which is mono-, di-, or tri-substituted with $R_C$;

$R_A$ and $R_B$, which may be the same or different, are independently selected at each occurrence from the group consisting of:

hydrogen, straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, (cycloalkyl)alkyl groups consisting of [3]4 to [8]12 carbon atoms, straight, branched, or cyclic alkenyl groups consisting of 2 to 8 carbon atoms, and straight or branched alkynyl groups consisting of 2 to 8 carbon atoms, each of which may be further substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, nitro, cyano, $C_{1-6}$alkoxy, -NH($C_{1-6}$alkyl), -N($C_{1-6}$alkyl)( $C_{1-6}$alkyl), -NHC(=O)($C_{1-6}$alkyl), -N($C_{1-6}$alkyl)C(=O)($C_{1-6}$alkyl), and Z;

$R_C$ is independently selected at each occurrence from halogen, cyano, halo($C_{1-6}$)alkyl, halo($C_{1-6}$)alkoxy, hydroxy, amino, and $C_{1-6}$alkyl substituted with 0-2 $R_D$, $C_{2-6}$ alkenyl substituted with 0-2 $R_D$, $C_{2-6}$alkynyl substituted with 0-2 $R_D$, $C_{3-7}$cycloalkyl substituted with 0-2 $R_D$, ($C_{3-7}$cycloalkyl)$C_{1-4}$alkyl substituted with 0-2 $R_D$, $C_{1-6}$alkoxy substituted with 0-2 $R_D$, -NH($C_{1-6}$alkyl) substituted with 0-2 $R_D$, -N($C_{1-6}$alkyl)($C_{1-6}$alkyl) each $C_{1-4}$alkyl

independently substituted with 0-2 $R_D$, $-XR_A$, and Y, with the proviso that at least one of the positions ortho or para to the point of attachment of Ar to the pyrimidine ring shown in Formula A is substituted;

$R_D$ is independently selected at each occurrence the group consisting of halogen, hydroxy, cyano, $C_{1-4}$alkyl, $-O(C_{1-4}alkyl)$, $-NH(C_{1-4}alkyl)$, $-N(C_{1-4}alkyl)(C_{1-4}alkyl)$, $halo(C_{1-4})alkyl$, $halo(C_{1-4})alkoxy$, $CO(C_{1-4}alkyl)$, $CONH(C_{1-4}alkyl)$, $CON(C_{1-4}alkyl)(C_{1-4}alkyl)$, $-XR_A$, and Y;

X is independently selected at each occurrence from the group consisting of $-CH_2-$, $-CHR_B-$, -O-, -C(=O)-, -C(=O)O-, -NH-, $-NR_B-$, -C(=O)NH-, $-C(=O)NR_B-$, -NHC(=O)-, and $-NR_BC(=O)-$;

Y and Z are independently selected at each occurrence from the group consisting of: 3- to 7-membered carbocyclic and heterocyclic groups, which are saturated, unsaturated, or aromatic, which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, $C_{1-4}$alkyl, $-O(C_{1-4}alkyl)$, $-NH(C_{1-4}alkyl)$, and $-N(C_{1-4}alkyl)(C_{1-4}alkyl)$; and

n is 0,1, or 2.

13. (twice amended) A compound or salt according to claim 9, wherein:

Ar is phenyl mono-, di-, or tri-substituted with $R_C$,

$R_X$ and $R_Y$, which may be the same or different, are independently selected at each occurrence from

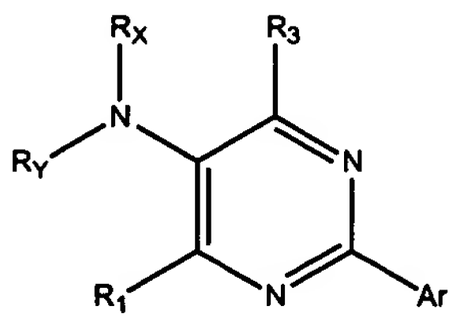
straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, (cycloalkyl)alkyl groups consisting of [3]4 to [8]12 carbon atoms, straight, branched, or cyclic alkenyl groups consisting of 2 to 8 carbon atoms, or straight or branched alkynyl groups consisting of 2 to 8 carbon atoms; and

$R_1$ and $R_3$ are independently selected from the group consisting of hydrogen, halogen, $C_{1-4}$alkoxy, $halo(C_{1-4})alkyl$, $(halo(C_{1-4})alkoxy$,

$C_{1-6}$alkyl, which $C_{1-6}$alkyl is unsubstituted or substituted by one to three substituents independently selected from hydroxy, oxo, cyano, $C_{1-4}$alkoxy, amino, and mono- or $di(C_{1-4})alkylamino$,

($C_{3-7}$cycloalkyl)$C_{1-4}$alkyl, which ($C_{3-7}$cycloalkyl)$C_{1-4}$alkyl is unsubstituted or substituted by one to three substituents independently selected from hydroxy, oxo, cyano, $C_{1-4}$alkoxy, amino, and mono- or di($C_{1-4}$)alkylamino.

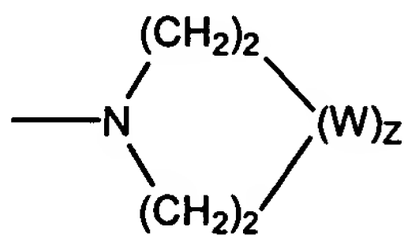
14. (amended) A compound or salt according to claim [3]9 of the formula:




$R_X$ and $R_Y$ are the same or different and are independently selected from the group consisting of:

hydrogen and $C_1 - C_6$ alkyl; or

$NR_XR_Y$ represents:

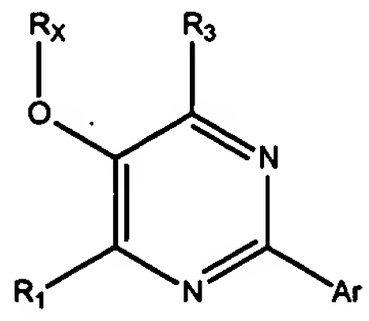



wherein:

z is 0 or 1; and

W is chosen from the group consisting of $CR_AR_B$, $NR_B$, and O.

15. (twice amended) A compound or salt according to [claim 3, of ]the formula




wherein:

$R_X$ is chosen from

straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, (cycloalkyl)alkyl groups consisting of [3]4 to [8]12 carbon atoms, straight, branched, or cyclic alkenyl groups consisting of 2 to 8 carbon atoms, or straight or branched alkynyl groups consisting of 2 to 8 carbon atoms, each of which may be further substituted with one or more substituent(s) independently selected from:

(a) hydroxy, halogen, amino, cyano, -O($C_{1-4}$alkyl), -NH($C_{1-4}$alkyl), and -NH($C_{1-4}$alkyl)($C_{1-4}$alkyl), and

(b) 3- to 7-membered carbocyclic and heterocyclic groups, which are saturated, unsaturated, or aromatic, which may be substituted with one or more substitutents selected from halogen, halo($C_{1-4}$)alkyl, oxo, hydroxy, amino, $C_{1-4}$alkyl, -O($C_{1-4}$alkyl), -NH($C_{1-4}$alkyl), –N($C_{1-4}$alkyl)($C_{1-4}$alkyl), wherein said 3- to 7-memberered heterocyclic groups contain one or more heteroatom(s) selected from N, O, and S, with the point of attachment being either carbon or nitrogen;

$R_1$ and $R_3$ are independently selected from hydrogen, halogen, cyano, $C_{1-6}$ alkyl, $C_{2-6}$alkenyl, $C_{2-6}$alkynyl, ($C_{3-7}$cycloalkyl$_1$)$C_{1-4}$alkyl, ($C_{3-7}$cycloalkyl$_1$)$C_{2-4}$alkenyl, ($C_{3-7}$cycloalkyl$_1$) $C_{2-4}$alkynyl, -O($C_{3-7}$cycloalkyl$_1$)$C_{1-4}$alkyl, -O($C_{3-7}$cycloalkyl$_1$)$C_{2-4}$alkenyl, -O($C_{3-7}$cycloalkyl$_1$) $C_{2-4}$alkynyl, halo($C_{1-6}$)alkyl, halo$C_{2-6}$alkenyl, halo$C_{2-6}$alkynyl, -O(halo($C_{1-6}$)alkyl), -O(halo($C_{2-6}$)alkenyl), -O(halo($C_{2-6}$)alkynyl), -O($C_{1-6}$alkyl), -O($C_{2-6}$alkenyl), -O($C_{2-6}$alkynyl), S(O)$_n$($C_{1-6}$alkyl, S(O)$_n$($C_{2-6}$alkenyl), and S(O)$_n$($C_{2-6}$alkynyl),

where each alkyl, or alkenyl is independently straight, branched, or cyclic, and each alkynyl is straight or branched, and is optionally substituted by one or more substituents independently chosen from halogen, hydroxy, oxo, cyano, $C_{1-4}$alkoxy, amino, and mono- or di($C_{1-4}$)alkylamino,

and

where said $C_{3-7}$cycloalkyl$_1$ is optionally substituted by one or more substituents independently chosen from halogen, hydroxy, oxo, cyano, $C_{1-4}$alkoxy, amino, and mono- or di($C_{1-4}$)alkylamino

with the proviso that not both $R_1$ and $R_3$ are hydrogen;

Ar is selected from the group consisting of phenyl, naphthyl, pyridyl, pyrimidinyl, and thiophenyl, each of which is mono-, di-, or tri-substituted with $R_C$;

$R_A$ and $R_B$, which may be the same or different, are independently selected at each occurrence from the group consisting of:

hydrogen, straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, (cycloalkyl)alkyl groups consisting of 4 to 12 carbon atoms, straight, branched, or cyclic alkenyl groups consisting of 2 to 8 carbon atoms, and straight or branched alkynyl groups consisting of 2 to 8 carbon atoms, each of which may be further substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, nitro, cyano, $C_{1-6}$alkoxy, -NH($C_{1-6}$alkyl), -N($C_{1-6}$alkyl)( $C_{1-6}$alkyl), -NHC(=O)($C_{1-6}$alkyl), -N($C_{1-6}$alkyl)C(=O)($C_{1-6}$alkyl), -NHS(O)$_n$($C_{1-6}$alkyl), -S(O)$_n$($C_{1-6}$ alkyl), -S(O)$_n$NH($C_{1-6}$alkyl), -S(O)$_n$N($C_{1-6}$ alkyl)($C_{1-6}$alkyl), and Z;

$R_C$ is independently selected at each occurrence from halogen, cyano, halo($C_{1-6}$)alkyl, halo($C_{1-6}$)alkoxy, hydroxy, amino, and $C_{1-6}$alkyl substituted with 0-2 $R_D$, $C_{2-6}$ alkenyl substituted with 0-2 $R_D$, $C_{2-6}$alkynyl substituted with 0-2 $R_D$, $C_{3-7}$cycloalkyl substituted with 0-2 $R_D$, ($C_{3-7}$cycloalkyl)$C_{1-4}$alkyl substituted with 0-2 $R_D$, $C_{1-6}$alkoxy substituted with 0-2 $R_D$, -NH($C_{1-6}$alkyl) substituted with 0-2 $R_D$, -N($C_{1-6}$alkyl)($C_{1-6}$alkyl) each $C_{1-4}$alkyl independently substituted with 0-2 $R_D$, -$XR_A$, and Y, with the proviso that at least one of the positions ortho or para to the point of attachment of Ar to the pyrimdine ring shown in Formula A is substituted;

$R_D$ is independently selected at each occurrence the group consisting of halogen, hydroxy, cyano, $C_{1-4}$alkyl, -O($C_{1-4}$alkyl), -NH($C_{1-4}$alkyl), -N($C_{1-4}$alkyl)($C_{1-4}$alkyl), -S(O)$_n$(alkyl) halo($C_{1-4}$)alkyl, halo($C_{1-4}$)alkoxy, CO($C_{1-4}$alkyl), CONH($C_{1-4}$alkyl), CON($C_{1-4}$alkyl)( $C_{1-4}$alkyl), -$XR_A$, and Y;

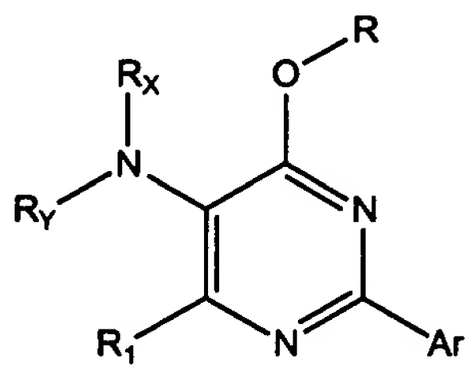
X is independently selected at each occurrence from the group consisting of -$CH_2$-, -$CHR_B$-, -O-, -C(=O)-, -C(=O)O-, -S(O)$_n$-, -NH-, -$NR_B$-, -C(=O)NH-, -C(=O)$NR_B$-, -S(O)$_n$NH-, -S(O)$_n$$NR_B$-, -OC(=S)S-, -NHC(=O)-, -$NR_B$C(=O)-, -NHS(O)$_n$-, -OSi$H_n$($C_{1-4}$-alkyl$_{2-n}$)-, and –$NR_B$S(O)$_n$-;

Y and Z are independently selected at each occurrence from the group consisting of: 3- to 7-membered carbocyclic and heterocyclic groups, which are saturated, unsaturated, or

aromatic, which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, $C_{1-4}$alkyl, -O($C_{1-4}$alkyl), -NH($C_{1-4}$alkyl), -N($C_{1-4}$alkyl)($C_{1-4}$alkyl), and -S(O)$_n$(alkyl); and

n is 0, 1, or 2.

17. (twice amended) A compound or salt according to Claim 3 of Formula B:




FORMULA B

Ar is phenyl mono-, di-, or tri-substituted with $R_C$;

R is selected from straight, branched, or cyclic alkyl groups, (cycloalkyl)alkyl groups, straight, branched, or cyclic alkenyl groups, or straight or branched alkynyl groups, and which are optionally substituted by one or more substituents independently chosen from oxo, hydroxy, halogen, cyano, -O($C_{1-4}$ alkyl), amino, -NH($C_{1-4}$ alkyl), and -N($C_{1-4}$ alkyl)($C_{1-4}$ alkyl);

$R_1$ is selected from hydrogen, halogen, cyano, $C_{1-4}$ alkyl, ($C_{3-7}$cycloalkyl)$C_{1-4}$alkyl, halo($C_{1-4}$)alkyl, halo($C_{1-4}$)alkoxy, and -O($C_{1-4}$alkyl); and

$R_X$ and $R_Y$ are the same or different and are independently selected from:

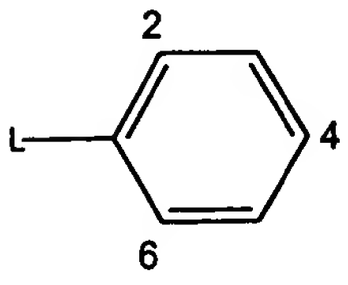
a) hydrogen,

b) -(C=O)alkyl$_A$, wherein alkyl$_A$ is a straight or branched alkyl group having from 1 to 8 carbon atoms;

c) straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, (cycloalkyl)alkyl groups consisting of [3]4 to [8]12 carbon atoms, straight, branched, or cyclic alkenyl groups consisting of 2 to 8 carbon atoms, or straight or branched alkynyl groups consisting of 2 to 8 carbon atoms, each of which may be further substituted with one or more substituent(s) independently selected from (i)hydroxy, halogen, amino, cyano, -O($C_{1-4}$alkyl), -NH($C_{1-4}$alkyl), and -NH($C_{1-}$

$_4$alkyl)($C_{1-4}$alkyl), and (ii)3- to 7-membered carbocyclic and heterocyclic groups, which are saturated, unsaturated, or aromatic, which may be substituted with one or more substitutents selected from halogen, halo($C_{1-4}$)alkyl, halo($C_{1-4}$)alkoxy, oxo, hydroxy, amino, $C_{1-4}$alkyl, -O($C_{1-4}$alkyl), -NH($C_{1-4}$alkyl), –N($C_{1-4}$alkyl)($C_{1-4}$alkyl), and -S(O)$_n$(alkyl), wherein said 3- to 7-memberered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S, with the point of attachment being either carbon or nitrogen.

19. (twice amended) A compound or salt according to Claim 17, wherein Ar is a phenyl group of the formula:




wherein L indicates a bond to the pyrimidine ring in Formula B

and the Ar phenyl group is substituted at one, two, or three of positions 2, 4, and 6 with substituents independently selected from:

i) halogen, cyano, halo($C_{1-4}$)alkyl, halo($C_{1-4}$)alkoxy, hydroxy, amino, $C_{1-6}$ alkyl, $C_{1-6}$alkoxy, ($C_{1-4}$alkoxy)$C_{1-4}$alkoxy, and mono- or di($C_{1-4}$alkyl)amino,

ii) $C_{1-6}$ alkyl and $C_{1-6}$alkoxy which are further substituted with a 3- to 7-membered carbocyclic and heterocyclic group, which is saturated, unsaturated, or aromatic, which 3- to 7-membered carbocyclic and heterocyclic group may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, $C_{1-4}$alkyl, -O($C_{1-4}$alkyl), -NH($C_{1-4}$alkyl), and -N($C_{1-4}$alkyl)($C_{1-4}$alkyl);

$R_X$ and $R_Y$ are the same or different and are independently selected from the group consisting of:

a) hydrogen (with the proviso that $R_x$ and $R_Y$ are not both hydrogen),

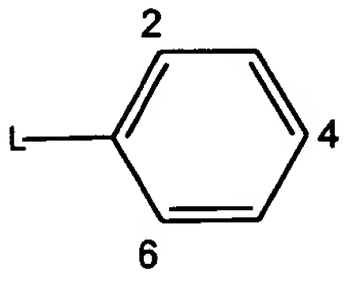
b) -(C=O)alkyl$_A$, wherein alkyl$_A$ is a straight or branched alkyl group having from 1 to 8 carbon atoms;

c) straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms,

(cycloalkyl)alkyl groups consisting of [3]4 to [8]12 carbon atoms, straight,

branched, or cyclic alkenyl groups consisting of 2 to 8 carbon atoms, or straight or branched alkynyl groups consisting of 2 to 8 carbon atoms, which may be further substituted with one or more substituent(s) independently selected from hydroxy, halogen, amino, cyano, -O($C_{1-4}$alkyl), -NH($C_{1-4}$alkyl), and -NH($C_{1-4}$alkyl)($C_{1-4}$alkyl).

20. (twice amended) A compound or salt according to Claim 17, wherein Ar is a phenyl group of the formula:




wherein L indicates a bond to the pyrimidine ring in Formula B

and the Ar phenyl group is substituted at one, two, or three of positions 2, 4, and 6 with substituents independently selected from:

i) halogen, cyano, halo($C_{1-4}$)alkyl, halo($C_{1-4}$)alkoxy, hydroxy, amino, $C_{1-6}$ alkyl, $C_{1-6}$alkoxy, ($C_{1-4}$alkoxy)$C_{1-4}$alkoxy, and mono- or di($C_{1-4}$alkyl)amino,

ii) $C_{1-6}$ alkyl and $C_{1-6}$alkoxy which are further substituted with a 3- to 7-membered carbocyclic and heterocyclic group, which is saturated, unsaturated, or aromatic, which 3- to 7-membered carbocyclic and heterocyclic group may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, $C_{1-4}$alkyl, -O($C_{1-4}$alkyl), -NH($C_{1-4}$alkyl), and -N($C_{1-4}$alkyl)($C_{1-4}$alkyl);

$R_X$ and $R_Y$ are the same or different and are independently selected from the group consisting of:

a) hydrogen (with the proviso that $R_x$ and $R_Y$ are not both hydrogen),

b) -(C=O)$alkyl_A$, wherein $alkyl_A$ is a straight or branched alkyl group having from 1 to 8 carbon atoms;

c) straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, (cycloalkyl)alkyl groups consisting of [3]4 to [8]12 carbon atoms, straight, branched, or cyclic alkenyl groups consisting of 2 to 8 carbon atoms, or straight or branched alkynyl groups consisting of 2 to 8 carbon atoms.